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THE STIMULATING AND ANTAGONISTIC ACTIONS OF THIOCYANATES AND AMMONIUM IONS

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Earlier work on the action of thiocyanates on isolated rabbit hearts made it possible to tabulate the results under eight headings: (1) concentrations of potassium, ammonium, and sodium thiocyanates which stimulated heart action, as evidenced by positive inotropic variations in the pulse; (2) concentrations producing both positive and negative inotropism; (3) concentrations producing only negative inotropism; (4) concentrations responsible only for facultative, temporary cessation of heart action; (5) the field of secondary inotropic effects; (6) concentrations causing primary contractures of the cardiac muscle; (7) concentrations causing (a) primary, obligatory cessations of heart action of various durations, (b) prolonged cessations but of a reversible nature; and (8) concentrations causing heart stoppage of an irreversible nature.

From the data under these headings it was concluded that the extent of the zone affected by stimulating concentrations was different for different thiocyanates. Thus, KCyS stimulates heart action in concentrations of about 0.1 "mg%"; NH_4.CyS in concentrations of from 0.1 to 3.2 mg%; while NaCyS acts as a stimulant, not only in concentrations of 0.1 to 3.39 mg%, but also, though with a weaker effect, in concentrations of 33.9 to 206.8 mg of this substance in 100 cubic centimeters of Ringer's solution.

The series KCyS $>$ NH_4.CyS $>$ NaCyS was established for the toxicity of these salts on rabbit hearts, and later also for mammals by studying the variations in blood pressure after introducing thiocyanates into the external jugular vein.

Based on the above findings it was proved that the extent of the zones of stimulating concentrations is inversely proportional to the toxicity of the individual thiocyanates.

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Starting with less toxic thiocyanates, it was proved that the extent of their zones of increasing, stimulating (not inactive!) concentrations is directly proportional to the degree of the harmlessness of the compound.

Stimulating and antagonistic unilateral action of ammonium ions. The stimulating effect of a one mg% solution of KCyS, added to Ringer's solution (without sodium carbonate), on a heart isolated by the Straub method and the positive inotropic effect of a one mg% solution of ammonium thiocyanate have been shown by graphs /not reproduced but available in original document in CIA/.

The stimulating action of NH_4.CyS took the form of a unilateral antagonistic effect on introducing it into a frog's heart previously poisoned with KCyS. The graphs show that the heart, after suspending activity on the introduction of one mg% of KCyS solution, resumed pulsation after introduction of one mg% of NH_4.CyS (in Ringer's solution). Ringer's solution alone failed to produce this effect. The same action occurred with 34 and 3.2 mg% solutions of ammonium thiocyanate after the heart was poisoned with 42.6 and 64 mg% of potassium thiocyanate and also (with the aid of 0.1 mg% NH_4.CyS) upon introduction of a 0.1 mg% solution of KCyS when the stimulating action of this concentration changed to an inhibitory action.

Potassium poisoning, caused by KCyS, can also be counteracted by $(NH_4)_2CO_3$, $(NH_4)HCO_3$ and certain other ammonium compounds.

Consequently, it seems probable that the unilateral, antagonistic effect in these cases is dependent on the ammonium cations, rather than on the various anions of these salts.

The same effect may be produced by certain ammonium compounds in poisoning by KCl in a concentration similar to that used by Hoeber in his experiments.

A heart poisoned by a one-percent solution of NaCyS also indicated reviviscence when treated with ammonium compounds.

In these cases it is evident that we can speak of the unilateral antagonistic action of the monovalent cation /NH_4/ on monovalent cations $K^\cdot$ and $Na^\cdot$. Very few cases of classical bilateral antagonism are known, generally speaking: the antagonism of $K^\cdot$ and $Na^\cdot$ and of $K^\cdot$ and $Li^\cdot$ are two instances.

A study of the relation of these cations to colloids, which would aid in explaining the stimulating action of ions and the antagonistic, unilateral action of ammonium ions on potassium and sodium poisoning, will be taken up in a future article.

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